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### Deposited in DRO:

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### Version of attached file:

Accepted Version

### Peer-review status of attached file:

Peer-reviewed

### Citation for published item:

Amabilino, David B. and Smith, David K. and Steed, Jonathan W. (2017) 'Supramolecular materials.', Chemical society reviews., 46 (9). pp. 2404-2420.

### Further information on publisher's website:

<https://doi.org/10.1039/C7CS00163K>

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# Supramolecular Materials

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Received (in XXX, XXX) 1st January 2017, Accepted 1st January 2017

First published on the web 1st January 2017

DOI: 10.1039/b000000x

Molecular material properties depend upon the contacts between and the arrangement of the component parts, and therefore supramolecular chemistry has developed a highly important role in this area. This Tutorial Review, after briefly introducing the history of the field, discusses some of the most exciting and inspiring recent achievements, with special focus on soft materials, particularly gels and liquid crystals.

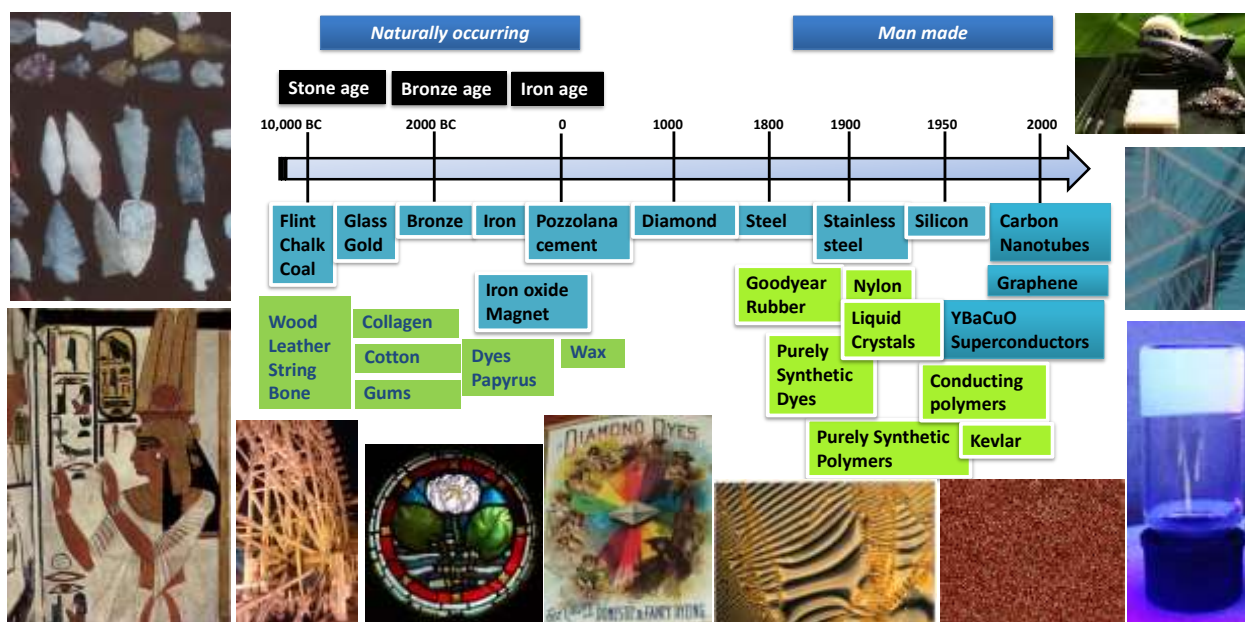
## Key Learning Points

- The interactions between the molecular components that determine the bulk behaviour of soft materials.
- Material structure and properties are an emergent, and often non-equilibrium outcome of the assembly.
- The dynamic nature of non-covalent bonds leads to novel properties like responsiveness and self-healing
- Both equilibrium and non-equilibrium assembly is subject can give functional materials by design.
- Supramolecular materials are an extremely promising and emerging area in materials chemistry.

## Introduction

Materials are transformational to the lives of the human race. They give the names to periods of history – stone, bronze, iron – because of their influence on our daily existence.

These hard materials were of course considered to be dominant for a long period, but in prehistory softer plant components – reeds, resins, stems and the like – were prevalent (Fig. 1). Indeed, because of their short lifetimes on the archaeological timescale, soft materials are the often forgotten component of human progress. Soft materials comprising molecule-based systems have gradually found applications in all kinds of everyday machines and devices, with supramolecular chemistry playing an increasingly evident role,<sup>1</sup> as it does in natural systems. For the Special Issue celebrating the anniversary of Supramolecular Chemistry, this Tutorial Review will introduce a personal selection of what we consider to be exemplary cases of particular materials where supramolecular chemistry has an important influence, the aim being to show the breadth of properties, principles and applications where the field has recently been deployed and where new paradigms are emerging.



**Fig. 1** A selection of materials through the ages: Photographs show (from top left) Ancient arrow heads, Queen Nefertari in a sheer, pleated linen garment, Egypt, ca. 1298–1235 BCE, wooden water wheel in Lanzhou, China, a stained glass window with inorganic dyes in Nottinghamshire, an advertisement for synthetic dyes from the USA, polarised optical micrographs of a liquid crystal and a synthetic fibre mesh, a modern soft material of plant origin; a nanocellulose hydrogel, organic dyes in a solar cell and the Nobel Museum exhibit of graphene.

The whole range of supramolecular interactions and combinations of them has been employed in the soft materials area, with certain types of material exploiting a particular type of interaction. Dipole-dipole interactions have proven influential in the assembly of dye molecules,<sup>2</sup> complementary hydrogen bonding is powerful for a whole range of exotic materials,<sup>[3]</sup> and the use of Coulombic interactions in “ionic self-assembly” can strongly direct structures and properties.<sup>[4,5]</sup> In the end, though, for a particular type of behaviour a material must be built using the supramolecular interactions that function best in that particular case, and for this reason here we separate the materials by the type of property for which they stand out.

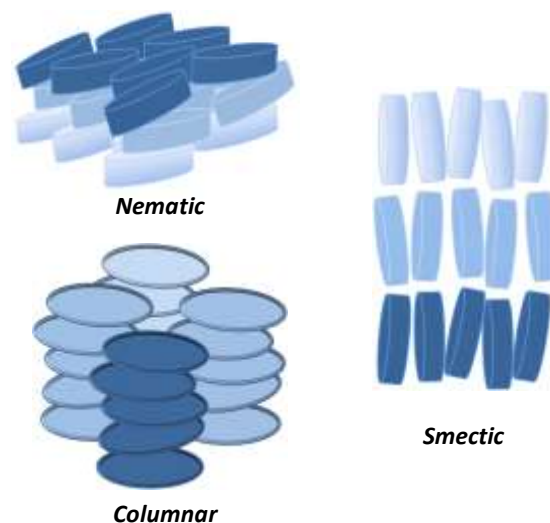
Before delving into specific cases, though, it is important to consider in which part of the thermodynamic profile a material is at when it has a particular structure and property: Materials can be close to their equilibrium state, but are often formed or exist far from it.<sup>6</sup> Moreover, materials properties are emergent and hence can depend on their structure and morphology and hence their history and formation mechanism. Let us first, then, put this in a materials context.

## Assembly: Equilibrium supramolecular materials

The aggregation of molecules under strict equilibrium self-assembly should lead predictably to a single structure under a given set of conditions.<sup>7</sup> If allowed long enough to equilibrate and with appropriate energy to allow mass transport, defects and metastable states are engulfed in the bulk stable phase, by the kind of process exemplified by Ostwald ripening. Liquid crystals – that are fluids with orientational order but positional disorder – are perhaps the materials with the broadest scope and application presently where the equilibrium structures are determined by the relatively weak interactions between molecules, though strong interactions can influence the shape and dimensions of the units that assemble to give the nematic, smectic or discotic phases (Fig. 2).<sup>8</sup>

Traditionally, these fluid materials have been purely organic, and certain design traits for the preparation of the equilibrium structures have been determined, such as the combination of rigid (crystal-like) regions and flexible (usually alkyl) chains. The incorporation of inorganic units is less developed perhaps, but new hybrid liquid crystalline materials can be prepared by combining suitable functional building blocks.

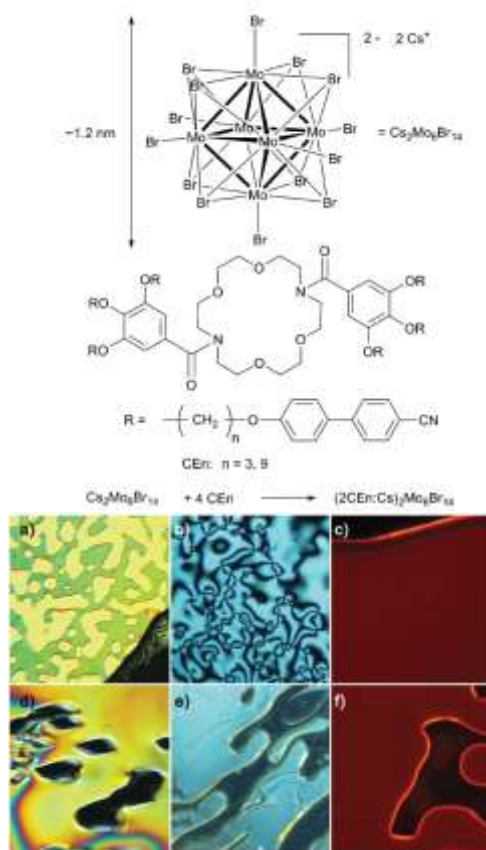
A particularly elegant recent example that shows the relatively straightforward marriage of nanometric inorganic anionic blocks with moieties typical in organic liquid crystals to give hybrid materials with the functionalities of both is that of the caesium salt of a molybdenum bromide cluster with an aza crown ether appended with promesogenic groups (Fig 3).<sup>[9]</sup> The main non-covalent interactions employed in the formation of the material are ion-dipole interactions between the alkali metal cation and the diaza-18-crown, electrostatic interactions between this complex and the molybdenum bromide cluster, and van der Waals interactions between the six cyanobiphenyl moieties. These latter groups are established promoters of liquid crystalline behaviour.



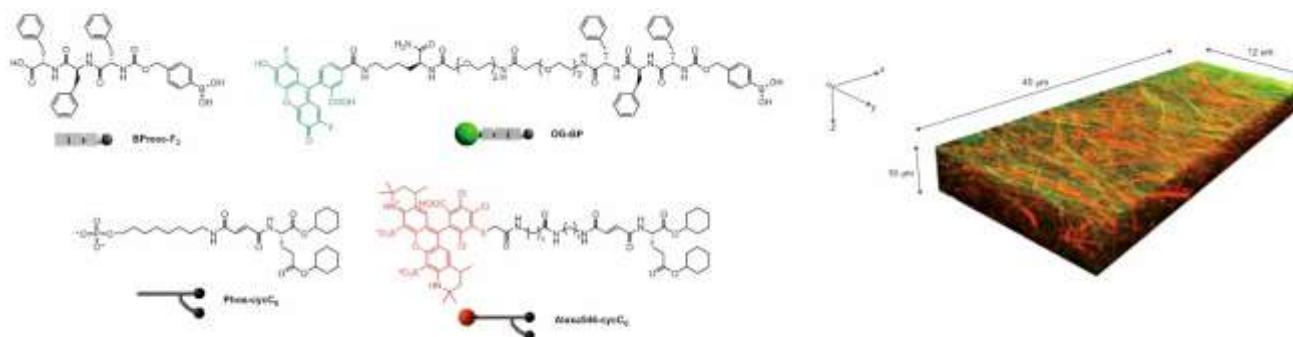
**Fig. 2** Cartoon representations of nematic and smectic packing of calamitic (rod-like) molecules or supramolecules and the columnar phase formed by disc like (supra)molecules.

The importance of the crown ether in the formation of the homogeneous material was proven by mixing the inorganic cluster with a simple mesogen devoid of the oligoether structure: phase separation resulted. The hybrids with three and nine carbon atoms between the cyanobiphenyl moieties and the aza group show nematic phases between 76 and 113 °C and 37 and 84 °C, only a little higher than the pure organic components. Both materials luminesce in the red. The micrographs of this effect demonstrate the homogeneity of the material, and with quantum yields that are similar to the pure materials. In this way, the supramolecular materials approach enables the fusion of liquid crystalline and inorganic materials properties – this approach is perhaps interesting for the preparation of equilibrium hybrid materials that can be processed reproducibly to give properties that are similar to the harder pure material. The long-term structural stability of molecular materials depends largely on whether they are near their thermodynamic minimum, equilibrium position, and therefore the preparation of systems close to this phase is of great interest.

A completely different approach to ionic liquid crystals has involved the novel use of halogen bonded anions to render imidazolium compounds into smectic liquid crystals.<sup>10</sup> The interaction between the iodide counter-anion from imidazolium derivatives with iodo-terminated linear fluorocarbons leads to a supramolecular anion with the general formula  $[C_nF_{2n+1}-I \cdots I \cdots I-C_nF_{2n+1}]^-$  which gives a material that is liquid crystalline at room temperature in certain cases. A crystal structure of one of the higher-melting salt complexes showed that the cations are nanophase segregated from the fluorocarbon, and the terminal iodine atoms of these chains interact with the iodide ion from the organic salt component. It is a unique example of liquid crystalline behaviour not being driven by the alkyl chains of the imidazolium cation. Even mixtures with the 1-ethyl-3-methylimidazolium cation form liquid crystalline materials.



**Fig. 3** Above, the chemical structure of a caesium salt of a molybdenum bromide cluster that forms a complex with the diazacrown ether derivatives indicated. Below, polarised optical micrographs obtained for (a) CE9 (45 °C), (b) and (c) (2CE9:Cs)2Mo6Br14 (80 °C, (b) white light, (c) UV irradiation), (d) CE3 (80 °C), (e) and (f) (2CE3:Cs)2Mo6Br14 (85 °C, (e) white light, (f) UV irradiation).



**Fig. 4** Structures of self-assembling systems investigated by Hamachi and co-workers, with the Three-dimensional CLSM image of the four-component mixture (BPmoc-F3/Phos-cycC6/OG-BP/Alexa546-cycC6). The three-dimensional CLSM image is constructed from z-stacked x-y slice images (Supplementary Movie 1). The scale of the z axis is compressed to one-third for clarity. Conditions: [BPmoc-F3] = 0.10 wt% (1.6 mM), [Phos-cycC6] = 0.10 wt% (1.6 mM), [OG-BP] = 0.0005 wt% (3.2 μM), [Alexa546-cycC6] = 0.0005 wt% (3.4 μM) in 100 mM MES buffer (pH 7.0).

## Assembly: Non-equilibrium supramolecular materials

The formation of materials can often result in structural phases that are not the absolute energetic minimum of the system, and under these conditions metastable, non-

Another way in which thermodynamic control of self-assembly can generate hybrid materials is to program molecular-scale building blocks with their own ‘information’ enabling each of them to self-assemble into its own unique nanostructures, with its own unique properties. In this way, directed assembly from mixtures can give rise to self-sorted materials. In elegant recent research, Hamachi and co-workers reported two different peptides, each of which was capable of self-assembly into a different type of supramolecular nanofibre.<sup>11</sup> By labelling each peptide with a different fluorescent probe, it was possible to use confocal laser scanning microscopy with super resolution (80 nm) to visualise differently coloured self-sorted fibres entangled in two and three dimensions (Fig. 4). In addition to the imaging providing outstanding visualisation of a self-sorted material, controlled by inherent self-assembly preferences, they then went on to use *in-situ* real-time imaging to investigate the kinetics of fibre growth kinetics. The two systems assembled with different kinetics – one assembling instantly (on the timescale of the experiment), while the other showed cooperative growth, enhanced by seeding. Importantly, the authors also observed both of the same kinetics processes in the growth of the self-sorted dual network – demonstrating that overall, the different fibres behave independently of one another, as programmed by the molecular scale interactions taking place. Understanding self-sorting processes in detail is of key importance, because mixing together two different self-assembling systems is an effective way of accessing systems which can exhibit different properties as a result of each network; providing access to enhanced function and applications of supramolecular materials.

equilibrium states that can display polymorphism can occur.<sup>[7]</sup> Polymorphism in crystalline molecular materials is well documented, and is relatively common in cases where various structures lie close in energy, with the preponderance of a particular form depending on the rate of nucleation and growth of each phase.<sup>[12]</sup> Polymorphism in nanomaterials is somewhat less well explored, although with appropriate

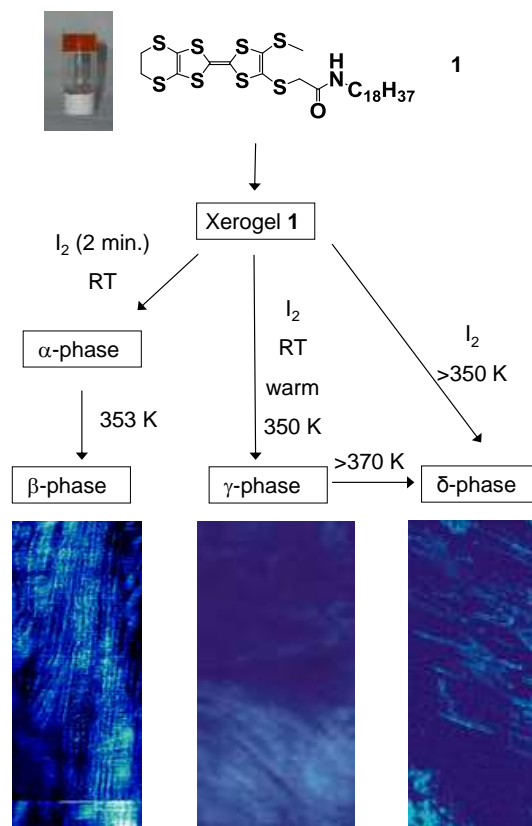


characterisation techniques it can be revealed.

Nanostructures are by their nature not the energy minimum state considering all of the components. They are usually trapped because of the presence of a deep energy well provided by stabilisation of interfaces between the multiple constituents. In the case of relatively simple systems, the barrier can be overcome by thermal treatment (or other means, such as solvent vapour annealing) and thereby new phases can be uncovered, as is the case<sup>13</sup> for oxidatively doped xerogels formed by the organogelator **1** (Fig. 4). The compound gels hexane through the formation of supramolecular polymers generated by the formation of hydrogen bonds between the secondary amine units, aided by  $\pi$ -stacking interactions between the aromatic system and van der Waals interactions between the alkyl chains of **1**. Upon evaporation of the solvent at room temperature the resulting xerogel (the solid remaining after liquid removal) can be doped with iodine vapour to partially convert the neutral form into the cation radical of the tetrathiafulvalene moiety, resulting in a conducting film. Warming of this film gives rise to a structural rearrangement of the fibres, witnessed by a decrease in resistance as well as a change in the electron paramagnetic resonance spectrum of the material, giving the second phase ( $\beta$ ). On the other hand, doping followed by immediate warming leads to a distinct structure ( $\gamma$ ) with a smooth texture and higher electronic dimensionality (as indicated by electron paramagnetic resonance spectroscopy), and further heating of this material generates a fourth polymorph with larger morphological features (observed by microscopy, see Fig. 5) and an even larger dimensionality. Therefore, the nanostructure that is present at room temperature, where individual supramolecular fibres are visible in the current sensing atomic force microscope images (Fig. 5) is gradually rearranged into distinct phases the structure and electronic transport of which are different. In this particular case the sensitivity of the conductivity to supramolecular packing changes in the material allowed a precise characterisation of the conversion of one phase into another, although at the present in other kinds of materials this can be more challenging.

A remarkable case of the formation of polymorphic nanostructures is that of the platinum(II) complex **2** (Fig. 6).<sup>14</sup> This class of neutral luminescent coordination compounds self-assemble through directional metallophilic intermolecular interactions with  $\pi$ - $\pi$  stacking between the ligand sections, the relative orientation determining the emissive properties. Most importantly, the intermolecular packing causes metal-to-ligand charge transfer states to be shifted (more bathochromically for the strongest inter-metal distance, or shortest distance, because of  $d_z^2$  interactions), making the emission position in the visible part of the spectrum an extremely sensitive indicator of supramolecular arrangement. For the particular case of the amphiphile **2**, with a triethylene glycol moiety affording hydrophilicity, spherical aggregates  $\alpha$  - approximately 126 nm in diameter - are formed in a water-dioxane 95:5 mixture. Indeed, this solvent mixture and its variation - which leads to a smooth variation of dielectric constant - is a great tool to study this particular system. The metastable spherical aggregates  $\alpha$  exhibit strong orange

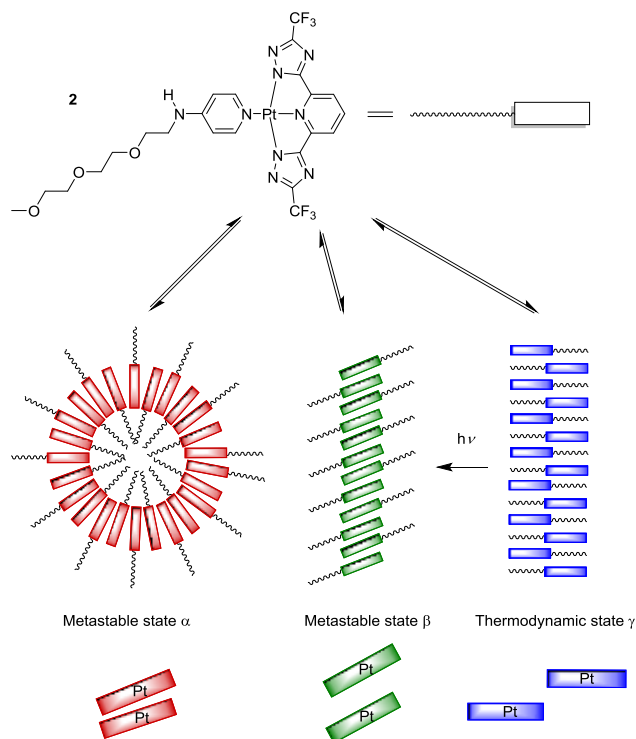
phosphorescence, and their conversion to the fibrous aggregates of the thermodynamically stable  $\gamma$  form results in blue emission.



**Fig. 5** A molecular gelator that when deposited to form a xerogel, doped with iodine vapours, and subjected to various heat treatments leads to four distinct material phases. The images are from conducting Atomic Force Microscopy, and the image dimensions are (from left to right) 0.2 x 0.5, 0.5 x 1 and 2 x 5 microns, and they show the increasing size of the domains formed during the hierarchical assembly that is accompanied by changes in the supramolecular structure.<sup>13</sup>

Photochemical measurements on **2** indicated an intermediate between these two aggregates, that was proven by fluorescence confocal microscopy to be the second metastable state  $\beta$ , also has a rod-like morphology but with a relatively small distance between the platinum complex moieties. The images showed that the rate of conversion between the forms, from  $\alpha$  through  $\beta$  to  $\gamma$ , is dependent on the solvent proportion. The process takes place at both 83 and 79% water but it is much faster at the lower percentage value, with a clearly greater nucleation rate and completion time, while longer objects were formed with the 83% mixture. Through variable concentration experiments the conversion of one polymorph to another was proven to proceed through the molecularly dissolved complex, as indicated in Figure 6; increasing the initial concentration of the  $\alpha$  form slows the inter-conversion. In addition, and uniquely, it is possible to convert completely the thermodynamically stable  $\gamma$  form into the metastable  $\beta$  polymorph by irradiating the sample with light for five minutes in a 95:5 water:dioxane mixture, a process that is believed to arise from energy transfer or

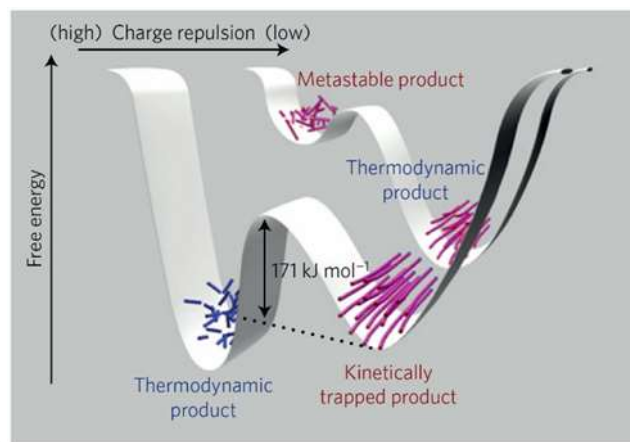
thermal effects. The result shows how a metastable form can be reached and converted to stable states, in a way that is reminiscent - albeit in a comparatively simple way - of some biological systems.



**Fig. 6** A platinum(II) complex that forms three polymorphic nanostructures in mixtures of dioxane and water. The diagrams at the bottom show in a very approximate way the distance between the metal ions in the chromophores, which determines their luminescence (indicated by the colours in these cartoons).<sup>14</sup>

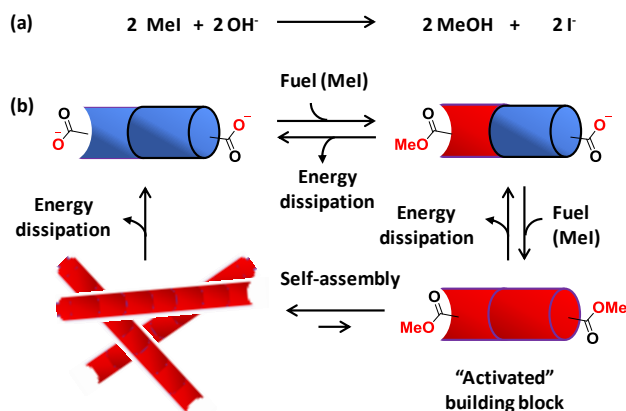
In very recent research, Stupp and co-workers very clearly expressed the important concept developed through the work described above – i.e., for supramolecular systems it is important to consider the whole ‘energy landscape’ potentially accessible to a self-assembled material, as this can be used to control the function of the overall system.<sup>15</sup> They initially employed a peptide amphiphile (PA) which forms hydrogen bonded  $\beta$ -sheets, and explored the response of its assembly to a number of parameters, specifically: (i) dilution, (ii) thermal annealing and (iii) addition of salt. They found that because of the energy landscapes for PA assembly (Fig. 7), they could access either a thermodynamic product, a metastable product, or a kinetically trapped product depending on the order in which the stimuli were applied. They also characterised the energy landscapes at both low and high ionic strengths, and the observed differences were attributed to screening of the charges on the PA favouring  $\beta$ -sheet formation at higher ionic strength. Importantly, by navigating through the energy landscape in different ways, it was noted that  $\beta$ -sheet formation could kinetically lock molecules in conformations that are thermodynamically unfavourable, and for this reason, changing the order of stimuli applied to the PA led to the different outcomes. To test the generality of this approach, the authors also studied chromophore amphiphiles held

together by  $\pi$ - $\pi$  interactions and demonstrated once again that the order of stimuli had a key influence. The authors went on to show that the PA materials formed using different approaches had different properties in terms of biological cell adhesion and survival. It is therefore clear that careful kinetic control over the assembly of supramolecular materials, which can be understood by detailed characterisation, can have a direct impact on the function and performance of the resulting material. This should not be underestimated when developing supramolecular materials – it is tempting to think of them in the equilibrium state, but very many of them have metastable, kinetic characteristics that mean the precise details of their formation histories will play a significant role in controlling their potential application futures.



**Fig. 7** Schematic representation of the free energy landscapes of peptide amphiphile self-assembly with relatively low (back) and high (front) charge-charge repulsions. At low intermolecular repulsion, long fibres with  $\beta$ -sheets are favoured and monodisperse short fibres represent a metastable state. At high repulsion, a kinetically trapped assembly and a thermodynamically favoured product separated by an energy barrier ( $E_b$ ) of 171 kJ mol<sup>-1</sup> were found. Figure reproduced from reference 17 with kind permission of Nature Publishing Group.

In addition to exploring the full energy landscape of supramolecular materials, it is possible to deliberately push supramolecular systems away from equilibrium. A different kind of metastable material is the a deliberately designed dissipative non-equilibrium supramolecular gel reported by the van Esch group in which consumption of a chemical fuel (MeI) maintains the system in an assembled state.<sup>16</sup> Reaction of a gelator precursor with methyl iodide results in methylation of the carboxylate groups to give a bis(methyl ester). This ‘activated building block’ undergoes self-assembly to give a gel (Fig. 8b). However, in the presence of base this gelator is continually undergoing hydrolysis to regenerate the carboxylate precursor. The methyl iodide fuel is therefore gradually consumed to give methanol according to the overall reaction given in Fig 8a. As a result the gel only persists as long as there is MeI “fuel” present to maintain the gelator in its activated state.



**Fig. 8** (a) The net reaction of one dissipative self-assembly cycle. (b) Reaction cycle of the dissipative system. The dicarboxylate (top left) can react with MeI (fuel) to give a monoester. This ester can dissipate its energy through hydrolysis to re-form the carboxylate precursor or react again with the fuel to form the activated building block diester. The diester can assemble into fibres, which are in equilibrium between formation and hydrolysis until all the MeI has reacted (reproduced with permission from ref. 16).

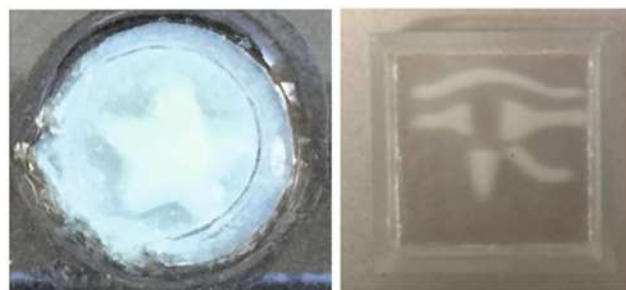
More recently, van Esch, Eelkema and co-workers extended this approach.<sup>17</sup> As previously, the authors used a reaction cycle between carboxylate anion (non-assembling) and methyl ester (capable of assembly), however, the ‘fuel’ for methylation in this case was dimethylsulfate, with base hydrolysis once again returning the system to the starting point. Importantly, the authors demonstrated through a series of careful studies that using different potential gelators, reaction rates and fuel levels, not equilibrium composition, that determined the behaviour of the system. The kinetics of the system were dependent on the concentration of fuel more than that of base, and that the gels formed were a kinetically controlled state. Importantly, the authors demonstrated that the lifetime, stiffness and self-regeneration capability of the self-assembled supramolecular fibres could all be programmed by the input of fuel – hence connecting function with fuel-driven assembly. Many biological systems, such as actin filament and microtubule assembly, are driven by the presence of a continuous supply of chemical ‘fuel’ in order to maintain assembly far away from equilibrium, and the authors noted that in this case, the fibres exhibited non-linear behaviour reminiscent of microtubule dynamics.

## Spatially-Resolved Supramolecular Materials

Given the interest in understanding and control of supramolecular materials in terms of their equilibrium and non-equilibrium assembly processes, there is increasing interest in controlling supramolecular materials in a spatially resolved manner – such that different domains of the material have different structures and hence different properties. This sets an interesting challenge – because most supramolecular materials are formed in the bulk solution phase, they generally simply fill the flask/vial in which they are formed and can retain this shape. Spatially resolved materials, would in principle have resolved mechanical properties and other

functions – this could lead to intriguing applications, for example in tissue engineering (see below), where spatial control is a desirable outcome. To achieve spatial resolution in supramolecular soft materials, the research groups of Adams and Smith have both recently turned to optical approaches employing photopatterning.

Adams and co-workers reported a two-component system in which both low-molecular-weight gelators could independently assemble into nanofibres on slow acidification of a basic aqueous solution.<sup>18</sup> They characterised the self-sorting of these gelators, which was enabled by a difference in the pKa values of the carboxylic acids leading to sequential protonation. After assembly of the self-sorted gel, one of the gelators containing a *trans*-stilbene unit could then be ‘switched off’ by UV irradiation, generating the non-assembling *cis* form (Fig. 9). This gel network could be disassembled in the presence of the other in the self-sorted material – lowering the *G'* value. Furthermore, by using a mask during the UV-irradiation step, this could be achieved in a spatially resolved manner, in which the unirradiated part of the gel still had both networks present, while the irradiated domain consisted of only a single gel network – the other network having been ‘etched away’. As such, spatial resolution of network density and rheological performance was achieved.



**Fig. 9** Spatially resolved multi-domain hydrogels produced from the research teams of Adams (left) and Smith (right) using ‘etching out’ and ‘writing in’ mechanisms respectively. Figure adapted from references 18 and 19 with the kind permission of Nature Publishing Group and American Chemical Society.

Smith and co-workers had also been working on photopatterning as a way of generating multidomain spatially resolved hybrid gels, for example writing a photo-crosslinkable polymer gel network into a supramolecular gel using UV irradiation and a photomask and went on to develop a system,<sup>19</sup> like that of Adams, which employed two self-sorting supramolecular gelators. However, Smith developed a ‘positive writing’ mode rather than ‘negative etching’ as used by Adams (Fig. 9). Once again, two low molecular weight gelators with different pKa values were employed. Just enough glucono-δ-lactone was added to protonate the first of these gelators, and assemble it into its fibre network, and then the second gelator was activated using diphenyliodonium nitrate, which is a photo-activated acid generator. Careful

NMR studies demonstrated that a good amount of self-sorting between the networks was achieved (ca. 80%). Furthermore, performing the photoactivation step under a mask gave rise to patterned materials in which the second gel network was written into the first. This was achieved with excellent resolution, with the presence of the first gel nanostructure limiting diffusion processes during the photo-irradiation step to create the second. Notably, pH indicators demonstrated that the pH only dropped below the second pKa value in those unmasked domains of the gel exposed to UV light. As such, in addition to having spatially resolved supramolecular materials domains, these systems also had spatially resolved pH profiles.

## Mechanical properties

Supramolecular materials have unique mechanical properties. In many cases, the key advantage of supramolecular systems is their ease of formation and their responsiveness to stimuli. However, this often leads to relatively weak mechanical performance, as the non-covalent interactions from which they are constructed mean they are often relatively easily broken down. For example, many supramolecular gels (also termed physical gels because of the reversible nature of their formation) are significantly weaker than their covalently crosslinked polymer gel analogues. Recently, in an influential review, Cornwell and Smith highlighted the advantages of combining low-molecular-weight and polymeric approaches to gelation, suggesting that an effective way of enhancing the mechanical performance of supramolecular materials was to use a secondary polymer network present as a reinforcing structural unit.<sup>20</sup> This strategy is increasingly being applied by researchers wanting to embed a functional supramolecular material within a more robust and resilient soft material.

In an interesting recent paper, however, Craig and co-workers made the intriguing observation that a supramolecular approach could also be used to enhance the strain resistance of covalent polymer gels.<sup>21</sup> In this work, a pyridine-functionalised polymer was permanently crosslinked through covalent reaction with a dibromide (1 per 50 pyridines), giving rise to a fragile polymer gel network. The gel was then exposed to a transient reversible supramolecular crosslinker through complexation with bi-functional Pt/Pd pincer complexes. It was noted that the covalent network contributed ca. 62–64 kPa to the modulus of each system, while the supramolecular component only added an extra 25%, and in one case, negligible additional modulus. However, as the gels were compressed further, the native gel broke at 103 kPa at the 80  $\mu\text{m s}^{-1}$  loading rate, while the presence of the supramolecular crosslinker led to dramatic (ca. 800%) increases up to 816 kPa under the same conditions. Importantly, the observed ‘strain-at-break’ was dependent on the loading of the supramolecular crosslinker, demonstrating this is the key component. Furthermore, even the supramolecular linker that did not increase the material modulus, had a significant effect on ‘strain-at-break’. As such, the authors reported that the supramolecular crosslinker could be ‘mechanically invisible’ yet have profound effects on the stress-strain behaviour. Supramolecular cross-linking

which is both thermodynamically and kinetically weak, leads to gels that are more deformable than comparable networks formed from stronger and slower interactions. It was suggested that the supramolecular topology might smooth out the stress distribution, limiting the stresses that initiate crack formation and propagation. It was noted that this feature is desirable for soft-active devices where high degrees of motion are desired.

In summary, it is clear that incorporating a supramolecular aspect into materials can be beneficial both for incorporating function and responsiveness into the overall system, but also for making significant, and sometimes unexpected, changes to the overall rheological performance. Furthermore, it is evident that the mechanical performance of hybrid materials will be the source of increasing interest. We therefore expect that many future studies will focus on the fertile ground of rheological characterisation and understanding of materials incorporating a supramolecular element.

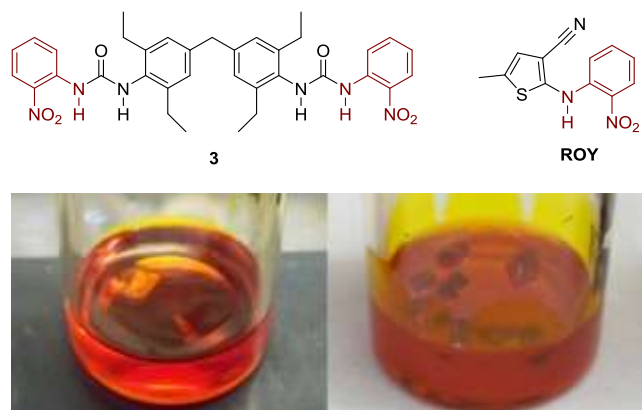
## Gel phase materials as crystallisation media

Gels have been used since the end of the 19<sup>th</sup> century as media for crystal growth. In the early years, hydrogels such as silica and agarose were used to produce well-formed crystals of inorganic salts. Perhaps the most famous work is that of Rafael Liesgang who, in 1896, added a drop of silver nitrate to a gelatin gel impregnated with potassium chromate. The result was a series of concentric rings of silver chromate precipitate termed ‘Liesgang rings’. The field of hydrogel crystal growth became popular again in the 1960’s as a means to produce high quality crystals for single crystal diffraction, particularly of protein samples. The role of the gels is to suppress convection currents, and limit sedimentation and nucleation as a result of the viscous gel environment. The gel is thus generally an inert matrix within which crystal growth occurs. Gels can, however, more actively influence the polymorphism, enantiomorphism and habit of crystals.

In the past decade there has been interest in the use of organogels as highly versatile crystallization media, particularly as a solid form discovery tool in pharmaceutical polymorphism. Steed and co-workers developed a bis(urea) gelator (**3**, Fig. 10) capable of gelating a range of relatively non-polar organic solvents such as toluene was designed to mimic the chemical structure of the olanzapine precursor ROY (so-called because of its ten red, orange and yellow polymorphs). The colouring in Figure 10 indicates the similar moieties. The ROY mimic gelator reproducibly resulted in crystallization of the metastable red polymorph of the substrate, while a range of control gelators chemically unrelated to ROY along with crystallization from solution under the same conditions gave the yellow conformational polymorph that is thermodynamically the most stable under ambient conditions.<sup>22</sup> Crystal structure calculation results suggest that the gel fibres mimic the conformation of molecules the red form more closely than those in the yellow form and hence the locally periodic gel fibre acts as a template for nucleation of this polymorph. This designer gel approach sits alongside a range of novel results in non-



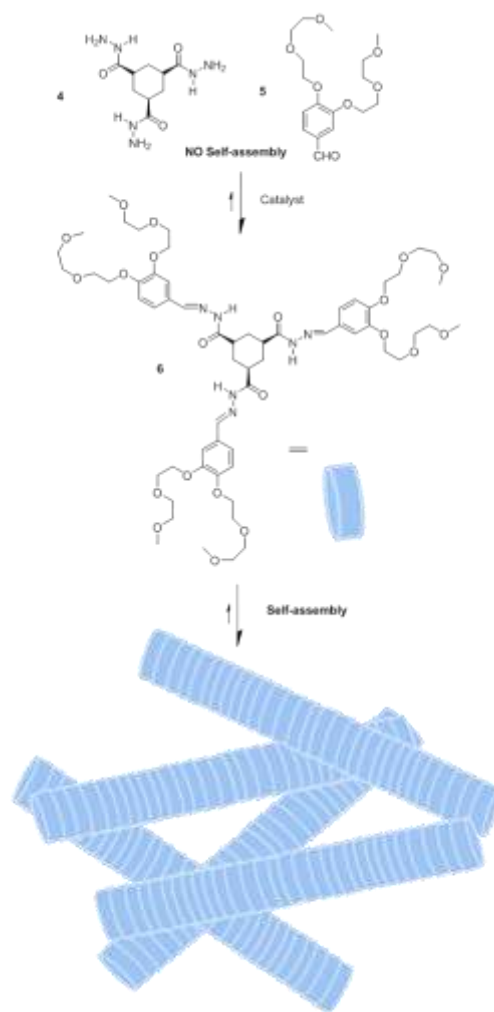
aqueous gel phase crystallization of small molecules including chirality control, and synergistic and antagonistic effects in multi-component dendron based gels in the crystallization of carbamazepine, aspirin and indomethacine that demonstrate that the gels take an active role in the crystallization process.<sup>23</sup>



**Fig. 10** Crystallization of the thermodynamic yellow form of ROY from a control gel unrelated to the substrate (left) and the metastable red form from a toluene gel of **3** (right).

## Catalytic control over supramolecular materials

Typically the formation of gel-phase materials is a relatively uncontrolled process relating to stochastic factors such as nucleation, growth, branching as well as external influences such as supersaturation, cooling rate and mass and heat transport. As a result gels are often metastable and their properties are, in some sense, emergent outcomes of their formation history. Work by the van Esch and Elkeema groups<sup>24</sup> has attempted to gain a measure of control over the outcome of the gelation process by controlled catalytic formation of the gelator molecule itself (Fig. 11). The amide group in the highly effective cyclohexane tris(amide) type gelators was replaced with a hydrolysable acyl hydrazine functional group. The resulting tris(acyl hydrazine) (**6**) can be produced by acid and nucleophilic aniline catalysis from soluble aldehyde (**5**) and tris(hydrazo) (**4**) precursors. Once formed, the gelator self-assembles into a fibrous hydrogel network. The gelation rate and the mechanical properties of the resulting material are highly dependent on the catalyst, with optimal conditions resulting in drastic enhancements of the rate at which the gelator is formed and of the resulting gel's mechanical strength – clearly indicating how controlling the formation of the self-assembling unit can impact on overall materials performance

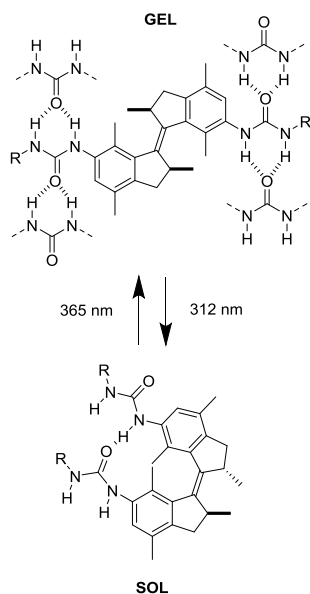


**Fig. 11** Concept of a catalysed gelator and gel formation. Catalytic formation of trishydrazone hydrogelator **6** from soluble building blocks **4** and **5** leads to supersaturation followed by fibre formation, which eventually crosslink to form a network that traps the surrounding solvent, leading to gelation.<sup>24</sup>

## Responsive materials

One of the most interesting attributes of supramolecular materials is their potential for responsive behaviour. The flexible and often dynamic nature of the intermolecular interactions in a soft material in particular suggests that the resulting structures may be able to adapt to a stimulus such as a chemical messenger or stimuli such as heat and light. Photoresponsive gel-phase materials are of particular interest because of the transparent nature of many gels, allowing good penetration of electromagnetic radiation. A simple and effective strategy to the design of photoresponsive gelators is to append gel-forming functionality such as the unidirectional hydrogen bonding offered by the urea moiety, to a photoresponsive core. This strategy gives rise to the sterically crowded bis(urea) gelator reported by Feringa and coworkers

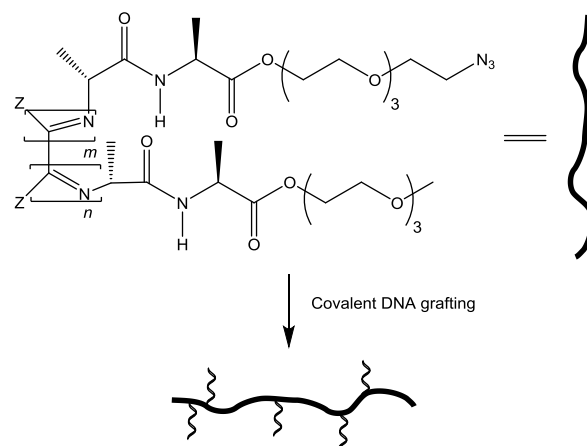
(Fig. 12).<sup>25</sup> In the *trans* form the compound is an effective gelator of organic solvents such as a toluene at quite low concentration (0.5 mg mL<sup>-1</sup>). X-ray crystallographic results confirm the formation of the well-known urea  $\alpha$ -tape hydrogen bonding motif, implicated in gel formation. Irradiation at 312 nm converts the compound to the intramolecularly hydrogen bonded *cis* form which is a non-gelator.



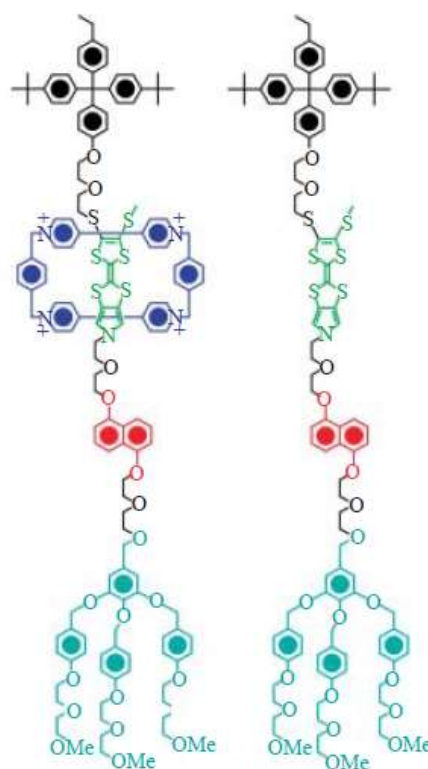
**Fig. 12** Reversible photo-induced *cis/trans* isomerism in a gelator resulting in photo-switchable immobilisation of solvent.

Another remarkable responsive type of hydrogel has been reported by Rowan and coworkers, based on a biomimetic polyisocyanopeptide motif that has recently been grafted onto DNA (Fig. 13).<sup>26</sup> The helical polymer is soluble in water thanks to the oligo(ethylene oxide) strands that are appended to amino acid residues that are responsible for the rigid secondary structure through amide hydrogen bonding between the side-chains. They form gels at extremely low concentration, down to 0.006 wt%, an order of magnitude less concentrated than other synthetic supergelators. The gels undergo a unique stress-stiffening type of mechanical response that mimics the behaviour of natural gels of cytoskeletal proteins. Unlike the natural materials, the structure of the polyisocyanopeptides can be readily varied allowing access to a broad range of highly tuneable biomimetic materials, like the grafting of DNA and cross-linking with complementary strand to affect the mechanical properties of the material.

A very different kind of responsive soft material is found in the first steps in making molecular computers. Work by Stoddart and Heath has allowed the construction of a 160-kilobit molecular electronic memory patterned at 10<sup>11</sup> bits per square centimetre.<sup>27</sup> The device is based on a monolayer of switchable [2]rotaxanes of the type shown in Figure 14, where the blue  $\pi$ -electron deficient ring is bound at the green  $\pi$ -electron rich site (in preference to the red one).



**Fig. 13** A co-poly(isocyanopeptide) artificial peptide that can be linked with DNA strands covalently and then combined with cross-linking DNA to give hydrogels.



**Fig. 14.** A [2]rotaxane and its dumbbell precursor that can be inserted into cross-bar electronic devices, derivatives of which have been used for extremely high density memory storage for the rotaxanes (kindly provided by Prof. Sir J.F. Stoddart).

The switching is achieved by oxidising the green unit and reducing the interaction of the ring with it. The films are made by preparing Langmuir layers of these molecules – the oligoethyleneoxy residues lie at the interface of the molecules with water, and the black hydrophobic end stands away from it – and then transferring them onto metal electrodes. It is important to note that the rotaxane is essential for function, as the component dumbbells do not show the same property. The

trapping of the ring on the rotaxanes is essential so that it does not simply diffuse away from the recognition sites. The devices of this kind are a first step in constructing a molecular switching based dynamic random access memory (DRAM) circuit. While the soft nature of the molecular 'bits' resulted in a large number of defects, it proved possible to isolate them and produce a fully functioning memory circuit capable of storing and retrieving information.

## Supramolecular Biomaterials

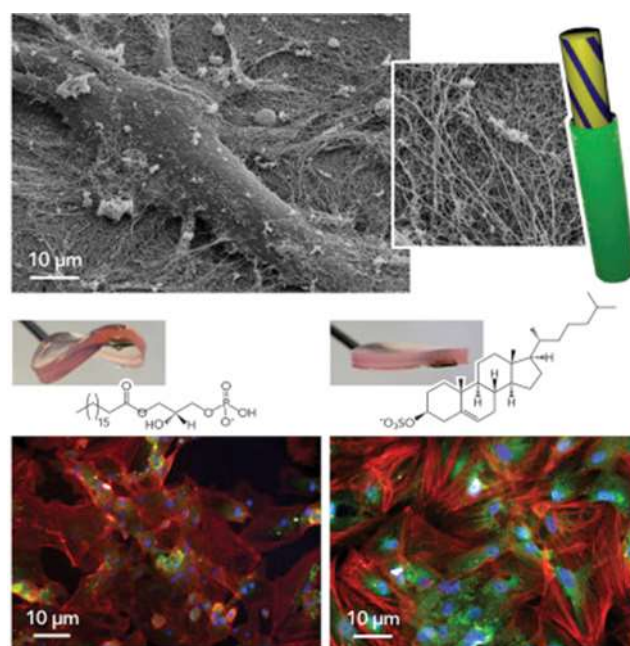
There has been considerable interest in the ability of self-assembled supramolecular materials to operate in a biological setting to address problems of biomedical importance. Indeed, an excellent review of early work in this area using gels has been published.<sup>28</sup> In particular, it is well established that self-assembled materials can be of great utility in controlling drug delivery processes (actively or passively) and enabling the growth and regeneration of cellular tissue (*ex vivo* or *in vivo*). This has led to eye-catching work in which supramolecular materials have been used (for example) *in vivo* to regenerate vision or spinal cord function by enabling the repair of damaged nerve tissue.<sup>29</sup> Researchers are now hunting for increasingly sophisticated ways in which supramolecular systems can intervene in such processes, and in particular, ways in which the chemical structures underpinning the systems control the behaviour of the material and the ways it can communicate with the biological environment.

Very recently, Ulijn, Dalby and co-workers provided an excellent demonstration of how supramolecular materials can be used both to direct tissue growth, and also to learn new valuable biological information (Fig. 15).<sup>30</sup> They created peptide hydrogels with simple compositions and tunable physical properties such that they had different stiffness (1 kPa [soft], 13 kPa [stiff] and 32 kPa [rigid]), and observed neuronal, chondrogenic and osteogenic stem cell differentiation respectively. Furthermore, by analysing the cell metabolites during differentiation on these gels, they were able to identify specific lipids that were depleted. Drawing the conclusion that these lipids were therefore vital in differentiation prompted them to perform 'feeding' experiments in which they showed these lipids can indeed induce differentiation in their own right. This innovative concept therefore not only achieves directed stem cell differentiation on a supramolecular scaffold, but also uses this approach to uncover new bioactive metabolites of potential therapeutic relevance. This could be powerful in personalised medicine, with an individual's stem cells being studied in this way in order to determine optimal ways of intervening in their regeneration to treat a variety of pathologies.

Although gels have been quite widely explored for drug delivery,<sup>28</sup> this is not the case for solution phase supramolecular polymers. In a recent paper, Dankers, Albertazzi and co-workers reported the potential of PEGylated 1,3,5-benzenetricarboxamide for intracellular delivery.<sup>31</sup> They took advantage of the modular way in which such polymers assemble, by co-assembling different building blocks into the overall supramolecular polymer to tune its function – for example different ratios of cationic and neutral

monomers. They loaded the core of this system with a hydrophobic guest, and then bound the peripheral cationic groups to siRNA. It was clearly shown that both compounds could then be delivered into living cells and that the siRNA was had intracellular activity. Cytotoxicity was low, although there was scope for further optimisation. Clearly this work builds on well-known cationic lipid strategies to nucleic acid delivery, but the high constitutional tunability of supramolecular polymers combined with the ability to effectively control, for example, their chain length offers intriguing scope for future exploitation.

There is no doubt that many future applications of supramolecular chemistry lie at the biomedical interface.<sup>32</sup> Clearly research in this field is closely allied with other approaches based on either polymer and colloid science, but supramolecular systems have their own unique contribution to make, and we perceive a future where 'supramolecular thinking' is taken into account in the design, implementation and application of much nanoscale biomedical research.



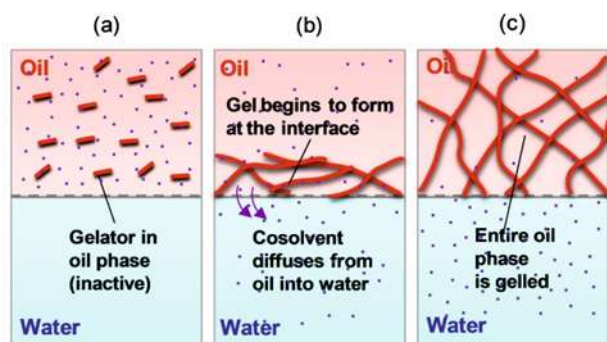
**Fig. 15.** Gels for tissue growth. A single MSC attached to the gel matrix (top left) which is constructed from self-assembled nanofibres (top right – including schematic). Stiff (centre left) and rigid (centre right) gels give rise to chondrogenic (bottom left) and osteogenic (bottom right) cell growth respectively, with different key lipids associated with differentiation being identified in each case. Image reproduced from reference 30 with kind permission of Cell Press.

## Environmental Materials

There has been considerable interest in applying supramolecular materials in an environmental setting for remediation of different types of pollution. Nanosystems have large inherent surface areas, and resulting high potential for adsorption of large quantities of unwanted contaminants.<sup>33</sup>

The concept of environmental remediation using a

supramolecular gel is beautifully exemplified by work from Raghavan and co-workers, who developed a gelator targeting limiting the loss of crude oil to the environment in the event of underwater pipeline damage.<sup>34</sup> In their research, a potential gelator (dibenzylidenesorbitol, DBS) was dissolved in toluene (as a model of crude oil), in the presence of small amounts of dimethylsulfoxide (DMSO) co-solvent which ensured the gelator readily soluble and hence inactive. This mixture was allowed to flow through a model pipeline. In the event of pipeline damage, the DMSO preferentially began to partition into the surrounding water, and the polarity of the crude oil phase dropped – initiating gelation of the DBS. This gel initially forms at the point of pipeline damage, and hence prevents further loss of oil to the environment. Importantly, this applied research builds on important fundamental breakthroughs in understanding the way in which supramolecular gels form in different solvents, with control of solubility being absolutely essential in triggering gel formation.<sup>35</sup> It was also noted that this mechanism for pipeline repair is somewhat mimetic of the way in which fibrinogen is activated to form clots in the event of wound damage to blood vessels in the human body.



**Fig. 16.** Concept for water-contact induced gelation of oil within a pipeline, as: (a) soluble gelator undergoes (b) a change in polarity on pipeline damage, until (c) gel formation has prevented the leakage from the pipeline. Figure reproduced from reference 34 with kind permission of the American Chemical Society.

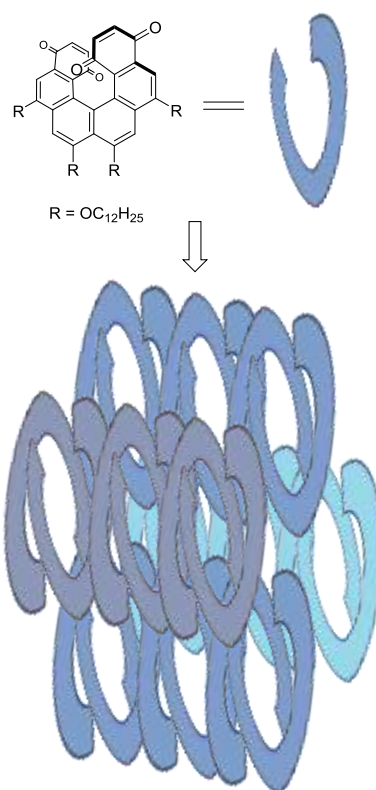
McNeil and co-workers recently developed a gel which was capable of detecting lead via a ‘switch-on’ gelation event, in which the formation of a lead complex, predicted by crystal morphology studies to be a potential gelator, underpinned the assembly of supramolecular gel nanofibres.<sup>36</sup> This gelation event could be triggered in the presence of paint samples containing lead contaminant (commonly present in older paints), and also from samples of dried paint which could be hazardous to human health if removed improperly.

In a key study, Smith and co-workers demonstrated that in addition to using a supramolecular material for environmental remediation, it may be possible to use the resulting product itself for a value-added application – from waste to wealth.<sup>37</sup> They employed an acyl hydrazide-functionalised dibenzylidenesorbitol which self-assembles into gel nanofibres in water, and demonstrated that it could selectively remove precious metals compared with other common metals

present in e-waste. The lower reduction potentials of the precious metals meant they were reduced into nanoparticle form, a process nucleated on the surface of the supramolecular nanofibres by the acyl hydrazide groups. In this way, Au(III) was converted into Au(0), Ag(I) into Ag(0) and Pd(II) and Pt(II) into Pd(0) and Pt(0), respectively. The gold nanoparticle embedded material was strengthened, by formulating it as a hybrid gel with agarose (see above for discussion of enhancing the mechanical performance of supramolecular materials), and then used as a modified electrode surface. It was demonstrated that the Au(0) nanoparticle embedded gel had a high conductance and was also an effective electrode surface, enhancing electrocatalysis. As such, the gold remediated using this approach could potentially be instantly used *in situ* in electronic applications.

## Optical Properties

The optical properties of molecular materials, ranging from absorbance and reflection to fluorescence or non-linear optical properties, depend critically on the supramolecular arrangement of the molecules in the bulk systems. The non-covalent bonds formed to chromophores as well as the relative disposition of identical  $\pi$ -functional moieties influence these properties, and therefore a wide range of effects can be observed for dyes under the influence of supramolecular chemistry.



**Fig. 17** A helicene molecule that shows a large increase in its nonlinear optical effect when deposited as layers on a substrate from a Langmuir trough.<sup>38</sup>

A classic and beautiful example of the influence of

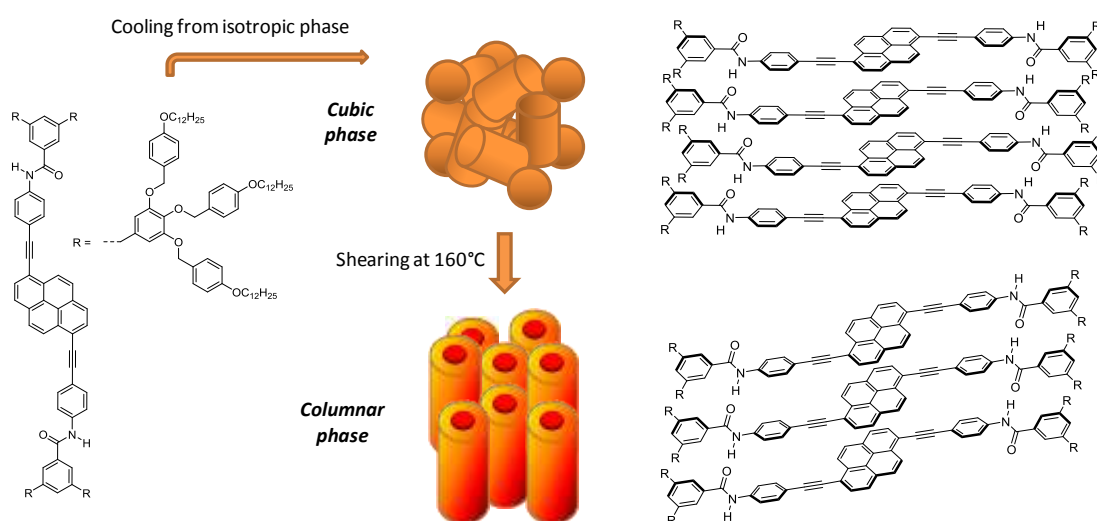


supramolecular organization on optical properties is that of the large enhancement of nonlinear optical properties in films of a helicene derivative,<sup>38</sup> where alignment of the molecules into columns (Fig. 17) lead to strong optical effects. The films of the helicene were prepared using a Langmuir trough with horizontal transfer of the compressed films onto different substrates. The Langmuir layers were prepared by spreading and subsequent evaporation of the solvent from chloroform solutions of the helicene on water. The compressed films were adhered to surfaces by horizontal dipping onto the layer (vertical dipping was also used to almost equal effect), and repeating this sequence several times to end up with a multilayer. The second harmonic generation (an indication of nonlinear optical properties) of light from the non-racemic films was around 1000 times that of the racemic sample, demonstrating that the effect is not molecular but a result of the organisation in the layers. Indeed, the order in the homochiral material is greater than in the racemic system, where shorter fibres are seen and no bundles of fibres are observed by atomic force microscopy, in contrast to the non-racemic material.

Intriguingly, macroscopic external forces can also be used to control the performance of these organised materials. The luminescence of liquid crystalline molecular materials - where the components have a pyrene core which is the optically functional unit - can be modulated through a change in the supramolecular structure when shear force is applied to the system in its fluid state.<sup>39</sup> The compound comprises dendritic extremities coupled through an amide linkage to the fluorescent core which has alkyne units to ensure rigidity but also rotational possibilities (Fig. 18). It displays a thermotropic cubic liquid crystalline phase between -35 and 175°C. This phase is optically isotropic, indicative of a cubic phase which was proven by diffraction experiments. The

structure of this phase comprises short stacks of molecules, and it fluoresces with a perceived yellow colour. Infrared spectroscopy indicated that hydrogen bonds link the molecules, with the C=O stretching band centred on 1655 cm<sup>-1</sup>. When a mechanical shear force is applied to the material in its cubic phase, a new phase is formed that is birefringent, shows blue-green fluorescence, and displays a C=O stretching band centred on 1645 cm<sup>-1</sup>. These observations, and especially X-ray diffraction experiments, indicated that a cubic to columnar phase transition had taken place, with stronger hydrogen bonds present in the newly formed phase thanks to the regular close packed structure. The effect is based on the transition of a metastable phase (the cubic one) to a more thermodynamically stable one (the columnar phase) by the isothermal activation with mechanical force, and is a kind of responsive material which can be converted once without thermal cycling. It is the polymorphic hydrogen bonding that makes this situation possible. Once again this indicates the subtle interplay between kinetics and thermodynamics in supramolecular materials.

The optical signature of chirality that is shown in circular dichroism (where one of the two hands of light is absorbed preferentially), for example, is of growing interest in particular for understanding supramolecular structure.<sup>40</sup> A beautiful recent example in which light is given out is in the area of circularly polarised electroluminescence that has been demonstrated using a platinahelicene.<sup>41</sup> Here, the coordination of the metal to the outer curved edge of a pyridyl substituted [4]-helicene is key to providing a sufficiently asymmetric environment to provide a remarkably high level of discrimination in the emission of handed light. There is great opportunity in these kinds of systems, because this particular case has a relatively low quantum yield.



**Fig. 18** Two of the components used to make a supramolecular glass and a cartoon indicating the proposed arrangement in the non-periodic superstructure.

## Electrical Properties

The transport of electrons through molecular systems is determined largely by the relative orientation of the functional units in the materials. This has been established in the charge transfer complexes and salts of molecular electron donors and acceptors and more recently in supramolecular systems such as that described earlier in this review using a hydrogen bonded chain.<sup>13</sup> In this case, the charge carriers were introduced by oxidising the tetrathiafulvalene unit with molecular iodine, that generates a mixed valence state where neutral and cation radical states of the electron donor are present. The initially-formed xerogel when doped is a relatively poor semiconductor, presumably because the order of the fibres once the solvent is removed. However, slight temperature annealing leads to a massive increase in conductivity. The dimensionality of the system can be increased by alternative annealing and doping processes, leading to four polymorphs observed to date (see Fig. 5) where the contacts between the fibres are enhanced. An area of potential interest with this kind of materials is in the preparation of chiral conductors that have been demonstrated to show intriguing physical properties recently.<sup>42</sup>

Alternating stacks of donor and acceptor molecules are not useful as conducting materials, but they can be exploited in other ways as a result of ordering of the charge transfer dipoles., especially in more ionic cases (where current flow is inhibited), because they can display ferroelectric behaviour at room temperature.<sup>43</sup> This property was shown by a group of crystalline organic ferroelectric materials resulting from intermolecular charge transfer. The particular crystals in question were formed by a  $\pi$ -electron deficient pyromellitic diimide compound bearing diethylene glycol-derived chains and one of three  $\pi$ -electron donors (diaminonaphthalene, diaminopyrene and bis(hydroxymethyl)tetrathiafulvalene). The main non-covalent bonding forces in the alternating stacks and between them in the solids are charge-transfer, hydrogen-bonding,  $\pi$ - $\pi$  stacking and van der Waals interactions. In particular, the hydrogen bonding cementing the superstructures takes place between the remnant diethylene glycol moieties of the electron acceptor and the amino or hydroxyl groups of the electron donors. Hirshfield analysis showed that 37–41% of all the inter-stack contacts arise from [O...H] hydrogen bonds while [H...H] contacts account for 42–50% of the total. In these complexes, a collective transfer of electrons from donor to acceptor leads to dipoles. The degree of charge transfer (indicated by the ionicity determined from polarised infrared spectroscopy) pointed towards a borderline ionic-neutral behaviour for the tetrathiafulvalene derivative donor, while the other two donor-acceptor complexes had mainly ionic character. Application of an external electric field can cause these dipoles to be reoriented, so that the molecules forming the stack end up switching their "partners". All three complexes displayed the phenomenon, even at room temperature, although the dielectric leakage and Joule heating affect the functioning that is observed much more nicely at low temperature (7 K). The remnant polarisation is greatest in the tetrathiafulvalene

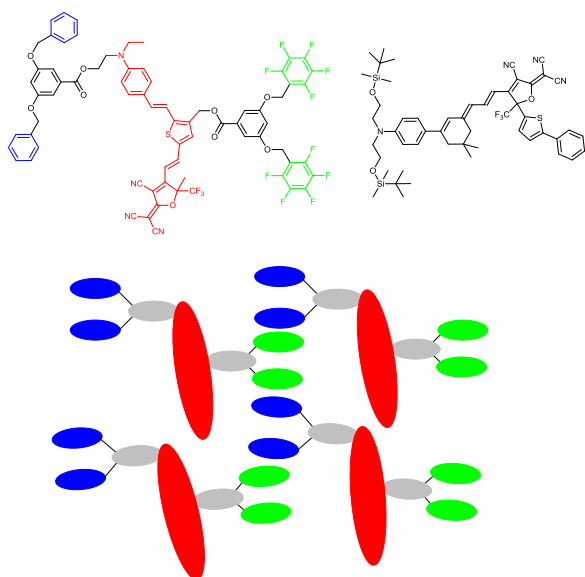
derived co-crystal, for reasons that are not abundantly clear at present, but which surely point to new discoveries and improved materials built on the foundation of this work and its forebears'. The shape of the supramolecular material (acicular crystals) is surely influential in the behaviour, and perhaps other processing methods for this kind of supramolecular system could prove beneficial. This family of materials is potentially interesting for use in sensors, photonics, energy-efficient memories and indeed anything that can exploit the easy and controlled switching between antiparallel orientations.

## Electro-optical Properties

The electro-optic effect most commonly studied (also known as Pockel's effect) involves the change in birefringence of a material upon applying an electric field to it. In molecular materials, this is achieved more often than not with non-linear optical chromophores.

The interaction between pentafluorophenyl groups and phenyl moieties on branched covalent donor-acceptor cores (Fig. 19) leads to molecular glasses that display large and thermally stable electro-optic effects.<sup>44</sup> The functional part of the molecules comprise units that have a large dipole moment.

The non-covalent intermolecular interactions between  $\pi$  electron deficient system and the more acceptor aromatic flanking groups serve to anchor the functional part of the molecules once the material is oriented using an electric field (that exploits the dipole of the molecules). While the formally donor-acceptor  $\pi$ - $\pi$  interactions do not apparently play a direct role in the property, the interaction between aromatic and fluoroaromatic groups have a dramatic effect on stability and robustness: The electro-optic activity is maintained (up to 90%) for two years, while the glasses without these interactions lost activity within a month. Therefore, the preference of dipoles to orient anti-parallel to one another has been overcome using non-covalent interactions to generate a polar material that is stable. When a second chromophore is incorporated into the glass, the order of this system is also maintained (Fig. 19). The electro-optic activity of these binary systems was the best observed for an organic material, and was ten times that of the best inorganic material, demonstrating the genuine potential of the supramolecular approach to enhance function.



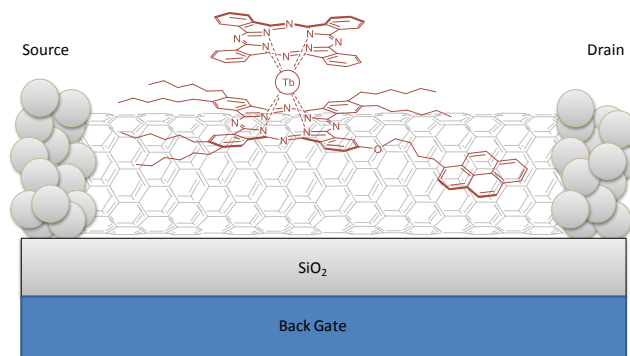
**Fig. 19** Two of the components used to make a supramolecular glass and a cartoon indicating the proposed arrangement in the non-periodic host superstructure formed by the molecule on the left (the molecule on the right would fill the voids in the network).

## Magnetic properties

The incorporation of units bearing unpaired electrons into molecular materials raises the possibility of the preparation of interesting magnetic molecular materials, where these spins can couple with one another in an either ferro-, ferri- or antiferro-magnetic way.

The limit of intermolecular exchange coupling between spins of electrons is always relatively low in molecular systems (they invariably require cryogenic temperatures for the magnetic exchange interactions to force ordering of the spins), at least until now. While the magnetic phenomena are fascinating, the physical limits of the coupling make rapid progress a significant challenge. However, interest in spin crossover and the burgeoning area of spintronics promises to revitalise the area of research.

An elegant example of a supramolecular spin valve was achieved by adhering a terbium(III)bis-phthalocyanine single molecule magnet onto a single-walled carbon nanotube incorporated through its ends into an electronic device (Fig. 20).<sup>45</sup> Magnetic memory has been transformed by the now standard giant magnetoresistance spin valves, where large changes in electrical conductance can be made by switching the relative magnetic orientation of the two conducting magnetic layers in the system. Conductance switches arise because of the different magnetic coercive values of the layers as an external field is applied. The supramolecular system achieved spin valve behaviour without magnetic leads, because of the quantum spin switching of the single molecule magnet (that has a large magnetic moment and anisotropy in its ground state thanks to the terbium ion).



**Fig. 20** A totally schematic view of a supramolecular spin valve device based on an asymmetric double decker terbium(III) bis phthalocyanine physisorbed onto a single walled carbon nanotube. In the actual device, about 100 nm separates source and drain electrodes and multiple molecules can physisorb to the tube.

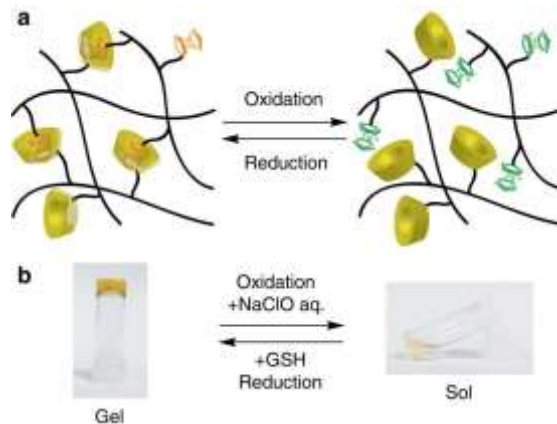
The design of the double decker terbium complex was such that specific adhesion of single molecules (rather than layers or stacks) to the carbon tube was attained, through the pyrene and hexyl substituents on one of the phthalocyanine rings that interact with the wire by  $\pi \cdots \pi$  and  $\text{C-H} \cdots \pi$  interactions. The asymmetry of the molecule also negated its crystallisation. Upon drop-casting of a solution of the molecule onto a prefabricated device incorporating the carbon nanotube between contacts, the molecular magnet settles on the tube such that the functionalised phthalocyanine ring achieves contact with the tube and has its plane parallel to the long axis of the adsorbent (Fig. 20). The orientation of the phthalocyanines was confirmed using magnetic measurements, from which it was clear that the easy axis of magnetisation (the favoured orientation of the molecules' spins that is at a right angle to the phthalocyanine planes) was perpendicular to the long axis of the nanotube. The electrical transport through the nanotube is affected by the localised magnetic moment of the adsorbant, the orientation of which is controlled by the external magnetic field, resulting in magnetoresistance ratios of up to 300%, albeit at less than 1 K. The work shows how bottom-up approaches, exploiting supramolecular programming in the components, can lead to functioning devices. Future challenges in this field will be to incorporate molecules in systems that can operate under accessible conditions for devices in everyday use.

## Healable and self-healing materials

In addition to their responsiveness, the dynamic nature of the bonding in soft materials offers the interesting possibility of self-healing behaviour in which the supramolecular nature of the interactions can re-form in the event of physical tearing or breakage of the integrity of the substance. This was nicely explored by Huang and co-workers who reported an influential example of a self-healing gel,<sup>46</sup> formed as a consequence of supramolecular cross-linking of a dibenzo-24-crown-8-functionalised polymer with ditopic bisammonium crosslinkers. Non-covalent interactions between the crosslinker and the polymer converted the system from a sol

to a gel, with the size of the ammonium cation appearing to control the kinetics of assembly process (the larger cation formed gels much more slowly). Rheological experiments demonstrated that the more rapidly assembled gel, with the smaller ammonium cation, re-healed in 30 seconds to 95% of its original mechanical performance – supramolecular self-healing. Intriguingly, however, the kinetically slower gel, rehealed in just ten seconds, even after the application of 10,000% strain. The authors proposed that some of the linkages in this latter system had become mechanically interlocked in a rotaxane-like mode, while other secondary interactions were unthreaded and could be rapidly formed and broken. It was proposed that this unique combination of kinetically trapped and thermodynamically reversible crosslinks gave rise to the remarkable self-healing behaviour. It is therefore clear that as well as considering equilibrium processes in the self-assembly of supramolecular materials, non-equilibrium events can also become highly significant.

In addition to their responsiveness, the dynamic nature of the bonding in soft materials offers the interesting possibility of self-healing behaviour in which the supramolecular nature of the interactions can re-form in the event of physical tearing or breakage of the integrity of the substance. Work by the Harada group has designed a series of cyclodextrin-functionalised hydrogel polymers based on polyacrylic acid (pAA) functionalised with either  $\beta$ -cyclodextrin (pAA- $\beta$ CD) to give a host polymer or with a redox-active ferrocenyl group to give a guest polymer (pAA-Fc).<sup>47</sup> The material forms effective, cross-linked hydrogels because of the affinity of the ferrocenyl guest for the cyclodextrin host cavity. This affinity is lost upon chemical or electrochemical oxidation of the ferrocene-derived substituent to the ferrocenium analogue (Fig. 21) resulting in redox-responsive gelation. The supramolecular nature of the ferrocenyl- $\beta$ CD interaction also results in highly effective self-healing behaviour. Cutting the gel with a razor blade and then placing the two cut faces in contact for 24 h resulted in re-formation of a single piece of gel with 84% of its original strength. The healing behaviour did not occur, however, in the presence of adamantane carboxylate, a competitive guest for the cyclodextrin cavity. Further, these researchers showed that two different materials based on either  $\alpha$ - or  $\beta$ -cyclodextrins could self-sort with materials based on two different guests and heal the interfaces between them – demonstrating how molecular-scale information can be used to direct materials healing on the macroscopic level.



**Fig. 21** (a) Schematic illustration of sol-gel transition on ferrocenyl-cyclodextrin materials. (b) Sol-gel transition experiment using chemical oxidant and reductant. Adding NaClO aq. to the pAA- $\beta$ CD/pAA-Fc hydrogel gives a phase transition into the sol state, and continuous addition of glutathione (GSH) to the sol yields a hydrogel again (reproduced with permission from ref. 47).

An alternative approach to self-healing materials has been proposed by Rowan and co-workers based on the conversion of light absorbed by a metal coordination complex into local heat. The material comprises macromonomers based on a rubbery, amorphous poly(ethylene-co-butylene) core appended with 2,6-bis(1'-methylbenzimidazolyl)pyridine ligands. These macromonomers are cross-linked into a polymer by  $\text{Zn}^{2+}$  coordination. Upon UV irradiation the ligands temporarily decomplex from the metal centre converting light energy into heat (Fig. 22). The resulting localised heating decreases the viscosity of the polymer film allowing for self-healing, followed by ligand recomplexation. The authors suggest that such photo-induced healing behaviour could be applied to repair specific regions of damage while the material is under load.<sup>48</sup>

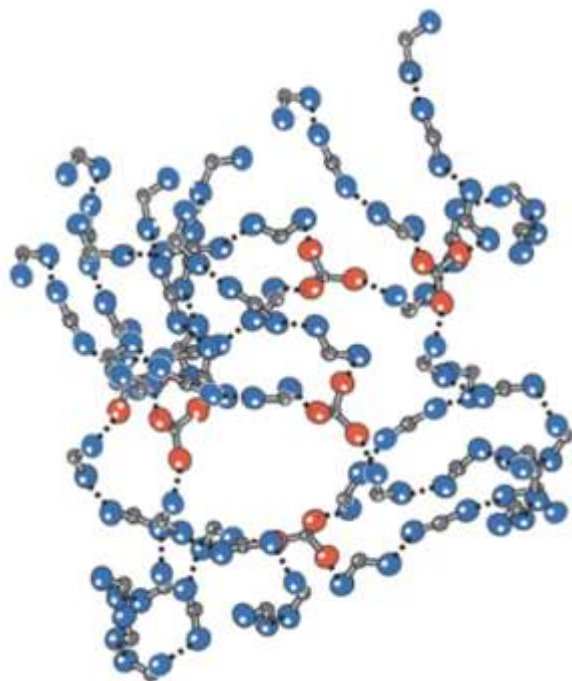


**Fig. 22** Proposed optical healing of a metallosupramolecular, phase-separated network (reproduced with permission from ref. 48).

A supramolecular approach to a self-healing rubber has been proposed by Cordier *et al.*<sup>49</sup> Conventional rubbers are able to extend to several hundred percent of their length and are based on a covalently cross-linked structure that does not self-heal when cut. By replacing covalent cross-links with non-covalent interactions a material can be produced that exhibits similar extensibility but also can be repaired when broken or cut by bringing the fractured surfaces together at room temperature. Remarkably the system also exhibits very little 'creep'. The self-healing rubber is based on a combination of a fatty diacid and triacid which are condensed



first with diethylene triamine and then reacted with urea giving a mixture of oligomers equipped with complementary hydrogen bonding functionality. The system then aggregates with hydrogen bonding cross links to give a supramolecular polymer, Fig. 23.



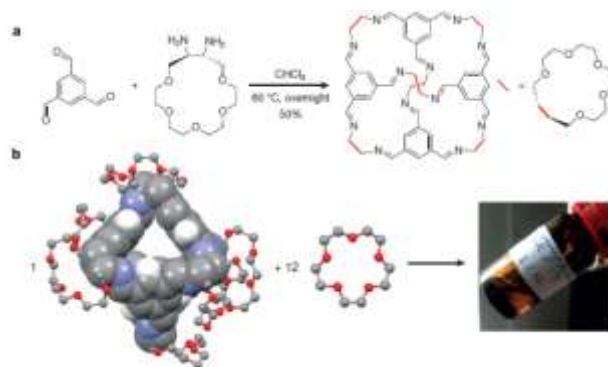
**Fig. 23** Schematic view of a reversible self-healing rubber network formed by mixtures of ditopic (blue) and tritopic (red) molecules associating by directional interactions (represented by dotted lines) (reproduced with permission from ref. 49).

Finally, it is worth noting that self-healing polymer technology has already found applications in self-healing smartphone coatings such as the G Flex and is tipped to be incorporated into touch sensitive screens in the near future.

## Porous Materials

A major field that has been transformed by replacing inorganic components with organic moieties is that of extended porous materials. The industrially very important aluminosilicate zeolites are limited in the structure types and pore shapes they can adopt by the relatively simple nature of their building blocks. In contrast metal-organic frameworks (MOFs) have revolutionised the field because of the infinity of ligands that can be used to generate them. MOFs are often crystalline hybrid materials with rigidly defined pores and are somewhat outside the scope of the present article which is concerned with soft materials. There has been however, one remarkable report of a very soft material with permanent porosity. Work by the Cooper and James groups showed that a porous liquid can be prepared from a solution of organic cage molecules derived from condensation of a crown ether diamine with a trialdehyde, in [15]crown-5 as a solvent (Fig.

24). This unusual solvent is sufficiently large that it does not fit into the intrinsic pore of the cavity and as the result is a liquid containing discrete, permanent 'pores' which are able to absorb (dissolve) guest molecules such as methane with a capacity around 8-times that of the neat solvent.<sup>50</sup>



**Fig. 24** Preparation of a porous liquid. (a), Synthesis of the crown-ether cage. (b) The empty, highly soluble cage molecule, left, defines the pore space; the [15]crown-5 solvent, middle, provides fluidity but cannot enter the cage cavities. The concentrated solution (porous liquid) flows at room temperature, right. The space-filling rendering highlights the core of the cage. Ball and stick rendering represents the crown-ether substituents on the cage and the 15-crown-5 solvent (reproduced with permission from ref. 50)..

## Conclusions

It is worth reflecting that in some ways the supramolecular approach to materials is a straightforward one. It is readily tunable at the molecular level, and in principle, information programmed into the molecular-scale building blocks can be translated through the nano- and micro-scales up to the macroscopic level. Furthermore, by controlling individual non-covalent interactions, the precision with which these materials can be manipulated is exquisite. Undoubtedly, this way of thinking about materials has much to add to the more traditional 20<sup>th</sup> Century ways of thinking about colloids and polymers – increasingly, supramolecular methods are being integrated into those other fields (and *vice versa*).

However, it is also worth noting that it can be tempting to consider supramolecular materials as being simpler than, in reality, they are. It is important to bear in mind that the material formed does not only depend on the molecular structures underpinning it, but also the way in which that material has been assembled – its history, and its environment. As molecules aggregate into supramolecular structures, systems become less reversible, and kinetic factors more important. Although this may seem challenging and complicated, in fact if characterised fully, such materials then offer a huge potential for developing more complex systems which can intervene precisely in processes of interest. Indeed, this simply offers another approach, in addition to the molecular one, by which these materials can be tuned and manipulated. Furthermore, the intriguing and unique

dynamics of supramolecular systems provide new ways of controlling the mechanical performance of materials and of developing systems with the capacity to self-heal and repair damage.

Most excitingly, the huge structural versatility of molecules which can underpin supramolecular materials, and the plethora of ways in which they can be put together, means a huge range of applications are within reach – from medicinal and environmental applications to opto-electronics and magnetic materials.

It is our hope that the personal selection of materials within this article will interest and inspire supramolecular chemists to create new systems with new properties, as well as prompting other materials scientists to consider whether incorporating a ‘supramolecular’ aspect to their system may allow them to “dial-in” the properties and function they desire. We hope readers will go on to read the indirectly cited work and learn from it, being stimulated to discover new phenomena and moving supramolecular materials forwards into the next generation of technologies.

## Notes and references

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